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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,992	10/22/2001	Joseph M. Patti	P06922US02/BAS	7767

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,992	PATTI ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,18 and 23-26* is/are pending in the application.

4a) Of the above claim(s) *1-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14, 18 and 23-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed November 17, 2003 has been entered. Claim 22 has been cancelled. Claims 1-14, 18 and 23-28 are under consideration.

2. A complete reply to the rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawal of Rejections

3. The following objections and rejections have been withdrawn in view of applicants' arguments:

a) The objection of claim 22;

b) The deposit rejection of claims 1-14, 18 and 22-26 under 35 U.S.C. 112, first paragraph;

c) The written description rejection of claims 10, 12 and 24 under 35 U.S.C. 112, first paragraph; and

d) The rejection of claim 2 under 35 U.S.C. 112, first paragraph.

Response to Arguments

4. Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The rejection of claims 1-4 under 35 U.S.C. 102(b) as being anticipated by Hook et al., (US Patent 5,648,240) is maintained for reasons already of record. The rejection was on the grounds that Hook et al., teach an isolated antibody that binds Map10 protein from *S. aureus*.

Applicants argue that Hook et al., relates to the cloning and sequencing of the whole MAP protein and not to the specific Map10 protein of the present invention. However, applicant is reminded that the claims are drawn to an antibody which binds the protein. Hook et al., teach antibodies that the protein, moreover Hook et al., teach antibodies that inhibit the binding of *S. aureus* just as the claims require. It is noted that applicants' arguments are not asserting that the antibody of Hook et al., and the antibody of the prior art are different. Applicants' arguments are not that the antibodies of Hook are not capable of preventing infection and suitable for administration. Applicants have provided no arguments to the issue of whether the antibodies of Hook et al., meet the limitations of the claims. Rather applicants have chosen to target the Map10 protein and state that Hook et al., did not isolate the same protein. This issue is not commensurate in scope to the claimed subject matter, which is the antibody and whether the antibody of Hook et al., reads upon the instant claims. Because applicants are silent on that issue, the rejection is maintained.

Since the Patent Office does not have the facilities for examining and comparing applicants' peptide with the peptide of the prior art reference, the burden is upon the applicants to show an unobvious distinction between the material structural and

functional characteristics of the claimed antibody of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

It is noted that the Prior art and instant specification use the same *S. aureus* bacterial species, isolated the same *map* gene, and create antibodies. Applicants' have provided no evidence that the variable binding regions on the antibody of the prior art is different than the region of the instant claims. Applicants have made no argument that the protein of Hook et al., bears different epitopes or binding regions as compared to the peptide of the instant application or that an epitope mapping analysis comparing the antibody of the prior art to the antibody of the instant claims differs. Thus, applicants' have not provided scientific evidence that the antibodies of Hook et al., will not bind the claimed protein. Therefore the rejection is maintained since applicants' arguments are not persuasive.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-14, 18 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. The claims are drawn to an isolated antibody which binds to the Map10 protein from *S. aureus*.

The generic claim language of claims does not adequately define: (a) species of antibodies, (b) the Map10 protein, and (c) Map10 proteins or degenerates thereof that fall within the realm of the claim. Accordingly, one of skill in the art cannot ready envisage the identity of the members of the genera. The written description in this case sets forth monoclonal antibody isotype H07 MAP.10 Mab IgG_1 and not any and all anti-Map10 antibodies capable of binding to Map10; preventing *S. aureus* infection; inhibiting binding of staphylococcal bacteria to eurkaryotic cells; and suitable for administration. The specification present evidence of monoclonal antibody isotype H07 MAP.10 Mab IgG_1, however the claims encompass all types of antibodies which bind to the Map10 protein, including antibodies undiscovered and/or unknown to have said binding ability. Furthermore, the target epitope has not been clearly identified on the Map10 protein and applicants are not in possession of all proteins containing the said target epitopes that anti-Map10 antibodies are capable of binding. The written description in this case only sets forth the specific antibodies listed on page 27 of the instant specification and all the antibodies do not have all the claimed characteristics.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Applicants are not required to disclose every species encompassed by a genus. For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Applicants broadly claim anti-Map10 antibodies which bind Map10 protein from *S. aureus*. However, Applicants are not entitled, nor is the specification enabled for the use of all anti-Map10 antibodies. Applicants are only in possession of 4 antibody species, which are not defined by structure and bind to Map10, see page 27. Applicants are not permitted to claim all antibodies that are encompassed by the claim language of the claims, hence not entitled to the wide breadth of the claims at issue. As Applicants' claims are written the recitation "an isolated antibody" could encompass not only as anti-Map10 antibodies, but variants as well. There is no description and no

information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others are excluded and missing from the disclosure, as well as features of the antigen.

Furthermore, the skilled artisan cannot envision the detailed structure of the encompassed antibodies and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. The claims drawn to antibodies that bind the Map10 protein contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention i.e., all antibodies that bind to the Map10 protein. Applicant has not demonstrated that any antibody that binds Map10 would be capable of preventing *S. aureus* infection and inhibiting binding of staphylococcal bacteria to eurkaryotic cells, thus applicants has not demonstrated possession of the generic inventions encompassed by these claims.

There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645; thereby the claims are rejected.

6. Claims 1-14, 18 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The genus encompasses antibodies that can bind variant Map10 proteins wherein such Map10 proteins have numerous differences in amino acid sequences, including numerous differences in linear and conformational epitopes.

However, the present specification fails to provide sufficient disclosure of such variant Map10 proteins which may or may not maintain the structural and functional properties of the Map10 protein. Additionally, the specification does not provide enabling disclosure that evidences the antibodies listed on page 27 facilitate activities presented in the claims, for instance as capable of preventing *S. aureus* infection and inhibiting binding of staphylococcal bacteria to eurkaryotic cells. The specification teaches that monoclonal H01 had no efficacy in the mouse bacteremia mouse models (page 29 para. [0060]). Moreover, the specification does not provide sufficient guidance as to which of the amino acids may be changed and still maintain the structural or functional activity and specificity required by the claims. It is noted that applicants teaching regarding specific Map10 antibodies is limited, yet the scope of the claims is quite broad. The claims read on any antibody that binds Map10 protein, including undiscovered antibodies or antibodies that are not currently known to have said binding ability.

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). For example, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

Because of this lack of guidance, the extended experimentation that would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al.; in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.), it would require an undue amount of experimentation for one of skill in the art to arrive at the other Map10 antibodies encompassed by the claimed invention.

The scope of the claimed Map10 specific antibodies is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of Map10 proteins broadly encompassed by the claimed invention. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's or peptide's amino acid sequence, and, in turn, nucleic acid sequence, and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e.

expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins/nucleic acids and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Thus, Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed Map10 antibodies in a manner reasonably correlated with the scope of the claims broadly including a broad number of structural changes encompassed by amino acid substitution variants of the Map10 protein. The scope of the claims must bear a reasonable correlation with the scope of enablement. See *In re Fisher*, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made are unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

7. Claims 1-14, 18 and 232-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Acronyms like Map10 and *S. aureus* must be spelled out when used for the first time in a chain of claims.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
March 15, 2004

MARK NAVARRO
PRIMARY EXAMINER